

Overview of Phorate

Revised Risk Assessment

September 2, 1999

Introduction

This document summarizes EPA's human health and ecological risk findings and conclusions for the organophosphate pesticide phorate, as presented fully in the documents, "Phorate: Revised HED Chapter for the Reregistration Eligibility Decision Document," dated September 2, 1999 and "Updated EFED RED Chapter for Phorate," dated August 30, 1999. The purpose of this summary is to assist the reader by identifying the key features and findings of these risk assessments, and to better understand the conclusions reached in the assessments.

The revised human health risk and ecological risk assessments for phorate will be posted on the Internet(<http://www.epa.gov/oppsrrd1/op/phorate.htm/>) and placed in the Pesticide Docket on or about September 2, 1999, and a 60 day public participation period on risk management will begin.

EPA has determined that it is appropriate to treat the organophosphates (OPs) as sharing a common mechanism of toxicity; the inhibition of cholinesterase activity. As required by FQPA, a cumulative assessment will need to be conducted to evaluate the risk from food, water and non-occupational exposure resulting from all uses of OPs. Currently, the Agency is developing the draft methodology needed to conduct such an assessment with guidance/advice provided by the Science Advisory Panel. It is anticipated that this draft methodology will be available in the late summer/early fall of 1999 for external comment and scientific peer review. Consequently, the risks summarized in this document are only for phorate.

Use Profile

- **Insecticide/Nematicide:** Registered for use on the following crops/sites: potatoes, corn (fresh sweet), peanuts, cotton, sugarcane, spring/winter wheat, soybeans, beans, sorghum and sugar beets. There are state registrations for lilies (field grown), daffodils and radishes grown for seed, however the registrant has not committed to supporting these uses.
- **Formulations:** Formulated as 6.5 %, 10%, 15% and 20% granular end-use formulations and 92-95 % emulsifiable concentrate manufacturing use product.

- **Methods of Application:** Aerial application; soil and foliar applications (band, broadcast, in-furrow and drilling).
- **Use Rates:** Use rates vary from a minimum of 0.66 lbs ai/acre to a maximum of 4.0 lbs ai/acre per application with a maximum of 2 applications per year.
- **Annual Poundage:** Estimated 3 million pounds used annually. Crops with the highest usage with reference to pounds produced are corn (45%), potatoes (24%) and cotton (15%). Almost 2.5 million acres are treated annually.
- **Registrant:** American Cyanamid

Human Health Risk Assessment

Revisions to the Preliminary Risk Assessment include

- The initial acute dietary risk assessment established a NOAEL based on a 1 year dog study. The revised risk assessment incorporates the results of a new rat acute neurotoxicity study which leads to the establishment of a new acute dietary endpoint.
- New dietary risk analyses utilizing a monte carlo (probabilistic) approach have been conducted by American Cyanamid and EPA to further characterize the acute risk assessment and to identify commodities that contribute most significantly to the risk. The acute dietary risk is below the EPA level of concern for all population subgroups .
- The preliminary occupational risk assessment was based on the use of an oral administration endpoint and a dermal absorption factor for exposures less than 28 days in duration. The revised occupational exposure and risk assessment considers a new subchronic dermal toxicity study on rats using a granular formulation; an occupational exposure study conducted with a similar chemical, terbufos, that reflects loading with a closed loading system and varying levels of PPE. The revised occupational risk assessment also took into consideration an occupational risk assessment prepared by the registrant. Worker risk is below the Agency's level of concern for all groups when using lock and load ground equipment and closed loading systems, personal protective equipment, and enclosed tractor cabs. Risks, however, are above the Agency's level of concern for all air applications.

Acute Dietary (Food) Risk

The Agency conducted a probabilistic (monte carlo) assessment that considers the distribution of food consumption values and the distribution of residue values found in food. A risk estimate that is less than 100% of the acute Population Adjusted Dose (aPAD, the dose at which an individual could be exposed on any given day and no adverse health effects would be expected, accounting for the safety factor) does not exceed the Agency's risk concern.

- The acute dietary risk (food) of phorate is below the Agency's level of concern for the general U.S. population and all population subgroups, including infants and children at the 99.9 percentile. The most highly exposed subgroup is children 1-6 with 70% of the acute Population Adjusted Dose (aPAD) consumed.
- End point is based on excessive contraction of the pupil observed in both sexes and a slight but statistically-significant decrease in brain cholinesterase activity in males in an acute neurotoxicity study in rats. The NOAEL is 0.25 mg/kg/day.
- Uncertainty Factor (UF) is 100 (10X for interspecies extrapolation and 10X for intraspecies variability). Developmental toxicity studies showed no increased susceptibility in fetuses as compared to maternal animals following *in utero* exposures in rats and rabbits. Similarly, the two generation rat reproductive data show no increased sensitivity in pups. A 3X FQPA safety factor was used to account for the lack of a subchronic neurotoxicity study. This study was recently submitted but not yet reviewed.
- The acute RfD is calculated to be 0.0025 mg/kg/day. The acute Population Adjusted Dose (aPAD), which is equal to the RfD/FQPA factor is 0.00083 mg/kg/day.
- The DEEM model was used to estimate acute dietary exposure. See table 1 (attached) for specific residue value inputs and assumptions used in estimating dietary exposure.
- Peanuts, potatoes and sweet corn contribute most significantly to the acute dietary risk for phorate.

Further Refinement

- The 3X safety factor was added because the subchronic neurotoxicity study was lacking. This study was submitted August 1999. Upon review of the study, the 3X decision will be revisited.

Chronic Dietary (Food) Risk

Chronic dietary risk is calculated by using the average consumption value for food and average residue values on those foods over a 70-year lifetime. A risk estimate that is less than 100% of the chronic Population Adjusted Dose (cPAD - the dose at which an individual could be exposed over the course of a lifetime and no adverse health effects would be expected, accounting for the safety factor) does not exceed the Agency's risk concern.

The chronic dietary risk for phorate does not exceed the Agency's level of concern (i.e., less than 100% of the chronic PAD is utilized) for all subpopulations at the 99.9th percentile. The most exposed subgroup is children (1-6 years), with 9.0% of the population adjusted dose consumed.

- End point is based on cholinesterase inhibition in RBCs and brain ChE activities in both sexes of a dog feeding study (NOAEL= 0.05mg/kg ; LOAEL= 0.25 mg/kg/day)
- Uncertainty Factor is 100. 10X for interspecies extrapolation and 10X for intraspecies variability. No increased susceptibility was noted in developmental and reproductive studies, however a 3X FQPA safety factor is used to account for the outstanding sub-chronic neurotoxicity data.
- The chronic Population Adjusted Dose (cPAD) is calculated to be 0.00017 mg/kg/day.
- The highly refined risk assessment was conducted using: **1)** % crop treated and **2)** anticipated residues determined from field trials. See table 1 for specifics

Further Refinements

- See Acute Dietary Risk Further Refinements section.

Drinking Water Dietary Risk

Drinking water exposure to pesticides can occur through groundwater and surface water contamination. EPA considers both acute (one day) and chronic (lifetime) drinking water risks and uses either modeling or actual monitoring data, if available, to estimate those risks. To determine the maximum allowable contribution of treated water allowed in the diet, EPA first looks at how much of the overall allowable risk is contributed by food, then determines a "drinking water level of comparison." Modeling estimates represent an upper bound on concentrations.

- Parent phorate is not likely to reach the water under most environmental conditions, based on the lack of persistence in soil and water and the lack of detections in limited sampling. The sulfoxide and sulfone metabolites which are more persistent and mobile in soil than parent phorate therefore are more likely to be present in water.

- Since there are no residential risks associated with phorate use, only the dietary risk from food is considered for purposes of calculating the DWLOC.
- Risk estimates for ground water are based on SCI-GROW modeling. SCI-GROW is a Tier 1 screening model that provides a high-end estimate. Since there is little degradation expected in ground water, one value is used for both acute and chronic estimates. For surface water, tier 2 estimated environmental concentrations (EECs) have been calculated for parent phorate and for total residues of concern (including parent phorate, and its sulfoxide and sulfone degradates) using PRZM (V3.12) and EXAMS (V2.975) models.
- For ground water, the maximum estimated concentrations of phorate and metabolites of concern is 13.5 ppb for peanuts, which represents the highest application rates. The maximum estimated concentration of phorate and metabolites in groundwater are greater than EPA's levels of comparison for phorate in drinking water as a contribution to chronic aggregate exposure. This is the same value used for the acute exposure since SCI-GROW modeling does not provide different values for acute and chronic estimated residue levels in water.
- For surface water using PRZM/EXAMS modeling, the estimated peak concentration of phorate and metabolites of concern in surface water is 27.6 ppb, and the annual mean is 1.6 ppb when used on cotton. The estimated surface water concentrations are less than or equal to the DWLOCs for chronic and acute risk.
- These estimates developed using conservative modeling indicate a potential risk concern may exist for phorate in drinking water for some subpopulations.

Table 1. Summary of Considerations Used in the Acute and Chronic Dietary Risk Analyses

Crop	Recommended Tolerance Reassessment, ppm	Acute Anticipated Residue Value, ppm ¹	Chronic Anticipated Residue Value, ppm	Percent Crop Treated	Processing Factors	Maximum Use Pattern Considered on Which the Dietary Exposure Assessment is based	Comments
Beans, dry	0.05	0.00075	0.00075	3	None	2.04 lb ai/A at planting	Used %CT x ½ LOQ. Insufficient information was available to determine LODs.
Beans, succulent	0.05	0.025, distribution	0.001	4	None	2.04 lb ai/A at planting, PHI = 60 days	All samples non-detect, so used ½ LOQ = 0.025 ppm for all “treated” samples. Insufficient information was available to determine LODs. Chronic AR = 0.025 x %CT.
Coffee	0.02	0.0006	0.0006	3	0.06 Roasting	(Not a U.S. use) 1 g ai/plant/year of plant life	Used tolerance x %CT. Insufficient information was available to determine LODs.
Corn, Field	0.05	0.00005	0.00005	1	refined oil 0.81	1.3 lb ai/A at planting and at cultivation PHI = 30 days	Used %CT x ½ LOQ. Insufficient information was available to confirm the LODs.
Corn, Sweet	0.05	0.05, distribution	0.01	20	None	1.3 lb ai/A at planting and at cultivation PHI = 30 days	Only four valid field trials, all detects - used proposed tolerance reassessment value for each detect due to the lack of data. Studies reflecting exaggerated rates were used for tolerance reassessment, but were not appropriate for use in risk assessment.
Cotton	0.05	0.0015	0.0015	6	None	1.64 lb ai/A at planting + 2.18 lb ai/A side dress PHI = 60 days.	All field trials non-detect. Used %CT x ½ LOQ. Insufficient information was available to determine LODs.

Crop	Recommended Tolerance Reassessment, ppm	Acute Anticipated Residue Value, ppm ¹	Chronic Anticipated Residue Value, ppm	Percent Crop Treated	Processing Factors	Maximum Use Pattern Considered on Which the Dietary Exposure Assessment is based	Comments
Peanuts	0.1	0.006	0.006	12	None	1.5 lb ai/A at planting; 3 lb ai/A at pegging. PHI = 90 days. Only one pegging treatment per season.	Used average of three field trials x the %CT. Residues were detected in all three field trials, reflecting PHIs from 70-90 days. Most 90-day PHI data reflected exaggerated rates and showed residues exceeding the proposed tolerance reassessment.
Potatoes	0.2	Distribution, 0.002 - 0.15	0.001	24	0.46 cooked 0.49 fried 0.46 boiled 0.26 peeled 0.44 peeled & cooked 0.27 peeled & boiled 1.2 dry	2.4-3.5 lb ai/A at planting or 2.3 lb ai/A post-emergence. PHI = 90 days	Thirteen field trials are available, four detects, and nine non-detects; used some ½ LOD and some ½ LOQ for non-detects. Chronic estimate = %CT x average residue value.
Grain Sorghum	0.05	0.00025	0.00025	1	None	1.3 lb ai/A at planting + 2 nd application at cultivation. PHI = 30 days	Used %CT x ½ LOQ. Insufficient information was available to determine LODs.
Soybeans	0.05	0.00005	0.00005	1	None	1.96 lb ai/A	Used %CT x ½ LOD. EPA estimate of LOD is 0.01.
Wheat	0.05	0.00015	0.00015	1	None	0.98 lb ai/A at planting. PHI = 70 days.	Used %CT x average of six field trials, three at ½ LOQ, and three at ½ the highest LOD.

NOTE: No residues were detected in sugarcane and sugar beets in processing studies, therefore no anticipated residue calculations were needed.

Residential Risk

There are no residential uses for phorate.

Aggregate Risk

Under the Food Quality Protection Act, the Agency considers contributions to risk from various exposure sources, specifically food, drinking water, and residential uses of a pesticide. There are no residential uses for phorate, therefore an aggregate assessment would only consider exposure from food and water.

- The Agency does not have sufficient reliable monitoring data to quantitate the risk from water, but conservative modeling information suggests that there may be a potential dietary risk contribution from water. The total dietary exposure from water and food sources cannot be combined for a total dietary or aggregate risk. The dietary risk from food sources alone are well below the Agency's level of concern for acute and chronic risk.

Occupational Risk

Workers can be exposed to a pesticide through mixing, loading, or applying a pesticide, and reentering a treated site. Worker risk is measured by a Margin of Exposure (MOE) which determines how close the occupational exposure comes to a No Observed Adverse Effect Level (NOAEL). For phorate, MOEs greater than 100 do not exceed the Agency's risk concern.

- Phorate is a restricted use pesticide.
- Phorate can be applied by aircraft and ground equipment (soil band treatment, soil in-furrow treatment, soil drill treatment, soil side dress treatment) to beans, corn, cotton, daffodils, lilies, peanuts, potatoes, sorghum, soybeans, sugar beets sugarcane, sweet corn and wheat. The maximum application rates range from 1.3 to 4.0 lb ai/acre (and 8 lb ai/A for bulbs only). Only one application per season is allowed for most uses. Two applications per season are allowed for irrigated cotton, sorghum, peanuts and sugar beets.
- The Agency has determined that there are potential exposures to workers as a result of mixing, loading, applying phorate, as well as flagger activities. Risk estimates have been derived for the following scenarios:

- (1a) loading granular formulations (completed using PHED data at varying levels of personal protection);
(1b) loading 20G formulation in “Lock-N-Load” packaging (completed using chemical-specific data);
(2a) applying granular formulations using ground-based equipment (completed using PHED data at varying levels of personal protection);
(2b) applying 20G formulation using in-the-row planters and closed tractor cabs (completed using chemical-specific data);
(3) applying granular formulations with aerial equipment (completed using PHED data only with closed cabs); and
(4) flagging for the application of granular formulations with aerial equipment (completed using PHED data at varying levels of personal protection)
- Phorate ranks high in the number of occupational incidents resulting in adverse health effects.

Short-Term and Intermediate-Term Occupational Risk

- Phorate use patterns show that both short-term (1 to 7 days) and intermediate term (1 week to several months) exposure is possible. .
- Short (1-7 days) and intermediate-term (7- 28 days) risks from dermal exposures to phorate were calculated using the endpoints from the recently submitted 28 day dermal toxicity study in rats. The NOAEL (No Observed Adverse Effect Level) observed in the 28 day dermal study for the 20G is 0.4 mg/kg/day which was used for exposure durations in the risk assessment up to 28 days.
- For intermediate-term exposures longer than 28 days, the Agency selected an endpoint from an oral administration chronic dog study of 0.05 mg/kg/day coupled with a dermal absorption factor of 100 percent.
- Chronic or long-term exposures (greater than 6 months) are not expected to occur with phorate.
- Short- and intermediate-term risks from dermal exposures to phorate were calculated using the recently submitted terbufos exposure monitoring study. The Agency used the terbufos data for the lock and load formulation but PHED for the open bag scenario. The exposure data from this study have been used in the phorate risk assessment (i.e., they have been used to bridge from terbufos to phorate) as is common Agency practice with occupational exposure monitoring data.

- Inhalation risks in this assessment were calculated using information from two different oral administration studies. The short-term assessment was completed using an endpoint of 0.25 mg/kg/day derived from an acute neurotoxicity study in rats where miosis and brain cholinesterase inhibition were noted. For the intermediate-term assessments, an endpoint of 0.05 mg/kg/day derived from a chronic study in dogs where red blood cell and brain cholinesterase inhibition were noted.
- Table 2 summarizes the occupational risk estimates for phorate. Based on these estimates, occupational risks do not exceed the Agency's level of concern when closed loading systems and personal protective equipment are used. If minimal PPE, open cabs, and products are loaded using bags that must be ripped open prior to loading, then risks exceed the Agency's level of concern.

Post Application Worker Risk

The Agency did not complete a quantitative assessment of post-application exposures to phorate because of when phorate is typically applied in the growing season and the way that phorate is applied (i.e., granulars that are soil incorporated).

Table 2. Summary of Phorate Occupational Risk Estimates

* Shaded blocks represent scenarios with MOE's > 100

Scenario	Exposure Data Source	Range of Combined Dermal and Inhalation MOEs ²		
		≤ 7 days Exposure ³	8-28 days ₄ Exposure	>28 days ₅ Exposure
Loaders (Assumptions: 69 to 213 acres treated, 90 to 360 lb ai handled daily, application rates 1-4 lb ai/A)				
Loading Clay Based Granules - BASELINE ⁶	PHED	7-28	4-14	1- 4
Loading Clay Based Granules - Minimum PPE ⁷	PHED	11-43	8-33	11-43
Loading Clay Based Granules - Maximum PPE ⁸	PHED	22-86	17-66	3-11
Loading Clay Based Granules for aerial application - Closed Loading System	chemical specific study	354-1419	178-714	48-193
Loading Clay Based Granules - Closed Loading System, Apron, Gloves, No Respirator	chemcial specific study	1220-4895	682-2739	162-652
Loading Clay Based Granules - Closed Loading System, Apron, Gloves, PF 10 Respirator	chemcial specific study	1482-5947	1353-5428	184-739
Applicators (Assumptions: 69 to 213 acres treated, 90 to 360 lb ai handled daily, application rates 1-4 lb ai/A)				
Applying Granular formulations with Ground-based Equipment - BASELINE ⁶	PHED	11-43	8-33	1-5
Applying Granular formulations with Ground-based Equipment - Minimum PPE ⁷	PHED	10 - 42	9 - 35	1 - 5
Applying Granular formulations with Ground-based Equipment - Maximum PPE ⁸	PHED	18-72	15-61	2-9
Applying Granular formulations with Ground-based Equipment - Enclosed Cab	PHED	32-129	20-82	4-17
Applying Granular formulations with Aerial Equipment - Enclosed Cab	PHED	21-83	6-26	3-13
Applying Granular formulations with Ground-based Equipment - Open Cab , Apron, Gloves, No Respirator	chemcial specific study	2022-8114	1440-5778	259-1040

Scenario	Exposure Data Source	Range of Combined Dermal and Inhalation MOEs ²		
		≤ 7 days Exposure ³	8-28 days ₄ Exposure	>28 days ₅ Exposure
Applying Granular formulations with Ground-based Equipment - Open Cab , Apron, Gloves, PF 10 Respirator	chemical specific study	2224-8926	2129-8546	275-1104
Combined Loader and Applicator (Assumptions: 69-213 acres treated, 90 to 360 lb ai handled daily, application rates 1-4 lb ai/A)				
Loading and Applying Granular formulations with Ground-based Equipment - Closed Loading System, Open Cab, Apron, Gloves, No Respirator	chemical specific study	761-3053	463-1858	100-401
Applying Granular formulations with Ground-based Equipment - Open Cab, Apron, Gloves, PF10 Respirator	chemical specific study	889-3569	827-3320	110-443
Flaggers (Assumptions:69-213 acres treated, 90-360 lb ai handled daily, application rates 1-4 lb ai/A)				
Flagging for Aerial Spray Operations - BASELINE ⁶	PHED	26-104	20-79	3-13
Flagging for Aerial Spray Operations - Minimum PPE ⁷	PHED	29-115	27-108	4-14
Flagging for Aerial Spray Operations - Maximum PPE ⁸	PHED	49-195	46-184	6-24
Flagging for Aerial Spray Operations - Engineering controls	PHED	1297-5205	382-3943	165-661

¹ Study data are of acceptable quality; most PHED data were of low quality with the exception of engineering control data, which were high quality.

² A Margin of Exposure (MOE) of greater than 100 is considered to be protective. Scenarios for which the MOE exceeded 100 for all exposure durations are highlighted.

³ Based on a dermal NOAEL of 0.41 mg/kg/day and a inhalation NOAEL of 0.25 mg/kg/day.

⁴ Based on a dermal NOAEL of 0.41 mg/kg/day and a inhalation NOAEL of 0.05 mg/kg/day.

⁵ Based on a dermal NOAEL of 0.05 mg/kg/day and a inhalation NOAEL of 0.05 mg/kg/day.

⁶ Baseline assessment assumes typical work clothing with no added protection.

⁷ Minimum PPE assumes use of gloves and a dust/mist respirator with a protection factor of 5.

⁸ Maximum PPE assumes use of double layer of clothing, gloves, and an air purifying respirator with a protection factor of 10.

Ecological Risk Assessment

To estimate potential ecological risk, EPA integrates the results of exposure and ecotoxicity using the quotient method. Risk quotients (RQs) are calculated by dividing exposure estimates by ecotoxicity values, both acute and chronic, for various wildlife species. RQs are then compared to levels of concern (LOCs). Generally, the higher the RQ, the greater the potential risk. Risk characterization provides further information on the likelihood of adverse effect occurring by considering the fate of the chemical in the environment, communities and species potentially at risk, their spatial and temporal distributions, and the nature of the effects observed in studies.

Historical Note

In December 1988, EPA sent a preliminary notification (i.e., Grassley-Allen letter) to American Cyanamid informing them that phorate was being considered for Special Review based on risk concerns to nontarget organisms, including birds, mammals and endangered species. A second Grassley-Allen letter was sent to the registrant in August 1990 indicating EPA's continued concern about risks to nontarget organisms and added risks to aquatic organisms as further basis for consideration of a Special Review.

Nontarget Terrestrial Animal Risk

Phorate is highly toxic to birds and small mammals when applied at label rates. There are indications that phorate may also pose a chronic risk to birds and mammals.

- Risk Quotient values greater than 1000 (acceptable RQ = 0.5) were obtained for mammals for broadcast applications for corn and hops, banded or in-furrow for potatoes, and banded or in-furrow for radishes.
- Avian RQ values ranged from about 600 for songbirds in broadcast use in corn and hops to 0.5 for upland game birds for soil in-furrow use in wheat. The risk quotient values suggest that songbirds are the most sensitive of the species tested.
- Several bird kills, some involving large numbers of birds, have been reported and linked to phorate use. Fall applications in the northern wheat growing states appear to pose a particular risk. During the winter in these regions, degradation and downward movement in soil is expected to be slow. The incident information indicates that in spring the concentrations of phorate and/or phorate degradates sometimes occurs at hazardous levels in pools on the soil surface.

Nontarget Aquatic Animal Risk

- Phorate is highly toxic to fish and invertebrates. Field studies and fish kill incidents confirm the risk predicted by the risk quotients

The level of concern for endangered species, both aquatic and terrestrial, on an acute and chronic basis is exceeded by use of phorate.

Summary of Pending Data

- Subchronic neurotoxicity study submitted August 1999.

Summary of Public Comments Comments

The Agency invited comments regarding the preliminary human health and ecological risk assessments for phorate. In response to the notice, a total of 24 comments were submitted to the phorate docket. The comments were from private citizens, trade groups/associations, non-government environmental organizations and American Cyanamid Company. American Cyanamid holds the registration for the active ingredient Phorate. Five of the 24 comments were considered specific to phorate. Four of those five comments were submitted by American Cyanamid. The fifth was submitted by the Northwest Potato Crop Protection Coalition (NPCPC). Cyanamid's comments generally involved revisions and refinements based on additional data they have agreed to submit to EPA. Comments from NPCPC involved information on use of phorate on potatoes.